Kidney International, Vol. 33 (1988), pp. 875–880

Role of renal hemodynamics in the exaggerated natriuresis of essential hypertension

PAOLO CORUZZI, LUISA MUSIARI, ALMERINA BIGGI, CARLO RAVANETTI, DANIELE VALLISA, ALBERTO MONTANARI, and ALMERICO NOVARINI

Istituto di Semeiotica Medica, Universersità degli Studi di Parma, Italy

Role of renal hemodynamics in the exaggerated natriuresis of essential hypertension. Extracellular fluid volume expansion is known to produce exaggerated natriuresis in essential hypertension. In order to assess the role of hemodynamic and intrarenal physical factors upon natriuretic response to central volume expansion, two hour water immersion (WI) experiments were made in six uncomplicated essential hypertensives and six normotensive healthy controls. Before and during WI we measured mean arterial pressure (MAP), urine flow (V/min), sodium ($U_{Na}V$) and potassium (U_KV) excretion, glomerular filtration rate (GFR), effective renal plasma flow (ERPF) and intrarenal (wedged) venous pressure (IRVP). In comparison with normotensive controls, the exaggerated natriuretic response in hypertensives ($P < 0.05$ for $U_{Na}V$ during WI) was associated with an enhanced vasodilating response as demonstrated by a greater increase in ERPF ($P < 0.05$) and by a more pronounced fall in calculated renal precapillary resistances ($P < 0.05$). A more significant increase in IRVP was found in hypertensive group ($P < 0.05$). Glomerular filtration rate (GFR) did not change in either group during WI. MAP, unchanged in normotensives, was significantly reduced in hypertensives ($P < 0.05$), while remaining in the hypertensive range. These findings suggest that intrarenal physical factors play a major role in determining the exaggerated natriuresis during WI in hypertensive man.

Abnormally high natriuretic response to acute extracellular fluid volume (ECFV) expansion has been extensively documented in arterial hypertension [1–3]. This so-called exaggerated natriuresis can be observed in hypertensive subjects during infusion of isotonic or hypertonic saline, mannitol or dextrose and water [1–5].

Both the very large fluid load and the subsequent changes in plasma composition may be avoided by using head-out water immersion (WI) in order to obtain isotonic-isooncotic central fluid volume expansion in man [6]. Indeed, recent studies have shown that hypertensives may also exhibit exaggerated natriuresis during WI [7, 8].

Experimental evidence has been accumulated from normotensive animals and humans suggesting that WI is associated with reduced renal vascular resistance and increased deep intrarenal venous pressure (IRVP) [9, 10]. These changes in the intrarenal physical factors may play a key role in determining the natriuretic response observed during WI. In the present study we examine the renal hemodynamics, and especially the IRVP behavior during ECFV expansion by WI in hypertensive man, in order to assess the importance of these factors in the "exaggerated natriuresis" phenomenon.

Received for publication December 9, 1986
and in revised form July 24 and November 12, 1987

Methods

Patients

We studied six male subjects with sustained essential hypertension (age range 25 to 45 years, mean body wt 76 ± 4 kg). The mean known duration of hypertension was three years (range 1 to 10 years). All of these were defined as having sustained arterial hypertension because their diastolic blood pressure was found to be consistently above 100 mm Hg on the fifth day of hospitalization and after 10 days withdrawal of any drug.

The diagnosis of essential hypertension was made according to the usual clinical, roentgenographic and laboratory tests to rule out any form of secondary hypertension. The patients had no major signs and symptoms of target organ damage. In only two patients moderate left ventricular hypertrophy, as assessed by standard criteria, was recognized.

The results were compared with our previously reported findings [10] in six healthy volunteer male subjects (age range 20 to 35 years, mean body wt 74 ± 3 kg). All these had a negative history for hypertension, cardiovascular disease and diabetes. Renal disease was excluded by documenting a normal urine sediment and creatinine clearance.

Methods

All subjects were put on a diet of constant sodium (150 mEq/day Na) and potassium (80 mEq/day K) content and the study was performed when the urinary sodium excretion equaled the intake; daily sodium output was monitored in 24 hour samples for five days prior to the test. The observations were made in the fasting state following 10 hours of fluid deprivation.

After a local anaesthesia with 1% lidocaine, percutaneous retrograde catheterization of the renal vein was performed by the method of Seldinger after puncture of right femoral vein: a polyethylene catheter (outside diameter 0.9 mm) was gently manipulated under fluoroscopy into a small division of the renal vein as far peripherally as possible. The criteria for a satisfactory intrarenal catheter position included a stable, clearly pulsating pressure curve at a level higher than renal venous pressure. Injection of minimal amounts of roentgen contrast

medium through the catheter disclosed the catheter tip located at the corticomedullary junction near the junction of the interlobar and arcuate veins. The vascular puncture site was protected by means of a sterile, waterproof, adhesive dressing (Tegaderm, Med. Prod. Division/3M, St. Paul, Minnesota, USA).

The immersion study started at 09.00 hours; the subjects voided and received 200 ml of tap water to drink. This water load was repeated hourly throughout the study in order to maintain adequate urine flow for the estimation of urine volume by spontaneous voiding. An antecubital vein was catheterized bilaterally for blood sampling and injection. Immediately after voiding a priming dose of inulin and p-aminohippurate (PAH) diluted in 0.9% saline was given into a forearm vein through an indwelling needle in amounts calculated to attain plasma levels of 25 and 1.5 mg/100 ml, respectively. Then, sustaining infusions of inulin and PAH were administered throughout the study utilizing an infusion pump at rates (0.5 ml/min) sufficient to maintain satisfactory plasma levels. After an equilibration period of 45 minutes, two basal, 30-minute clearance periods were performed (preimmersion study), followed by four 30-minute clearance periods (immersion study). The inulin and PAH clearance were calculated according to the method of Schnurr et al [11]. No correction was made for PAH renal extraction; thus our determinations are designed as "effective renal plasma flow" (ERPF). The subjects sat quietly outside of the immersion tank for one hour (preimmersion period), then the subjects stepped into the immersion tank and sat on a stool with water to the neck at constant temperature (34.5 ± 0.5°C) with their arms outside of the tank. The subjects remained in this tank for two hours and voided at hourly intervals.

At the end of each hour, before the subjects stood to void, 10 ml of blood was drawn for the estimation of osmolarity, plasma proteins and hematocrit. The hourly urine volumes were measured and the concentrations of sodium and potassium were determined.

Deep renal vein pressures were measured with a Statham pressure transducer (the renal hilus was used as the zero reference level) and recorded on a multichannel photographic recorder (Battaglia Rangoni, Bologna, Italy); the pressure curves did not change with respect to preset levels after the subjects had moved for voiding. Blood arterial pressure was measured non-invasively every five minutes with an automatic blood pressure monitor (Arteriosonde Roche, model 1225, Basel, Switzerland) and every 10 minutes with a standard mercury manometer.

Urinary sodium and potassium were determined with a flame photometer.

Inulin was termined colorimetrically according to anthrone method of Young and Raisz [12] and PAH by method of Smith et al [13]. The values for the individual clearance period were corrected to 1.73 m^2 body surface area and the mean value for the preimmersion period and the immersion period was calculated.

Filtration fraction (FF) was calculated as the C_{In}/C_{PAH} ratio (%); hematocrit was measured using a hematocrit centrifuge. Afferent arteriolar plasma protein concentration (C_A) was defined as the plasma concentration in peripheral venous blood; efferent arteriolar plasma protein concentration (C_E) was calculated from the filtration fraction and from C_A using the relationship $C_E = C_A/1 - FF$. Values for afferent (Π_A) and efferent (Π_E) plasma oncotic pressures were then derived from C_A and C_E using the relationship: Π (mm Hg) = 1.629 C + 0.2935 C^2 [14].

Table 1. Clinical and laboratory findings in six control and six hypertensive subjects at the day prior to the water immersion study

		Body weight *kg*	Age *years*	Mean arterial pressure *mm Hg*	24-H our urinary sodium excretion *mmol*
Control subjects	1	72	32	87	171
	2	74	35	97	173
	3	76	20	93	130
	4	77	33	90	141
	5	71	20	85	104
	6	74	35	98	153
Mean ± SEM		74 ± 1	29 ± 3	92 ± 1	145 ± 4
Hypertensive patients	1	80	42	130	176
	2	76	45	140	138
	3	72	36	117	150
	4	70	25	143	161
	5	78	45	130	158
	6	79	30	127	170
Mean ± SEM		76 ± 2	37 ± 3	131 ± 2	159 ± 2

In the calculation of the renal vascular resistance the following equation was used [15]:

$$\text{precapillary resistance} = \frac{\text{MAP} - \text{IRVP (mm Hg)}}{\text{RBF (ml/min)}} \times 8 \times 10^4 \text{ (dyne} \cdot \text{sec} \cdot \text{cm}^{-5})$$

where MAP is mean arterial pressure, IRVP is intrarenal venous pressure and RBF is renal blood flow, obtaind by dividing ERPF for (1-hematocrit).

Statistical calculations were carried out with the non-parametric Wilcoxon matched pairs sign-rank test and the Mann Whitney U-test for comparisons between groups. The null hypothesis was rejected when $P \leq 0.05$. In the presentation of the data, mean values are followed by the SEM as an index of dispersion. The purpose of the study, the experimental procedure and its possible risk factors were explained to the subjects. No complications, such as air embolism, infection, thrombosis, hemorrhage or dye reactions occurred. The protocol has been approved by the Ethical Committee at the Institute of Semeiotica Medica. The investigation has been conducted in conformity with the basic principles embodied in the Declaration of Helsinki.

Results

Table 1 shows some clinical and laboratory findings in control and hypertensive subjects.

Urine flow (V/min) and urinary excretion of sodium ($U_{Na}V$) and potassium (U_KV) were similar in hypertensive patients and controls during the preimmersion period (Table 2). During WI, the increase in $U_{Na}V$ was significantly greater in hypertensives. The peak value of $U_{Na}V$ was reached during the second hour of WI in both groups: it was 535 ± 15 μmol/min (range 503 to 600) in hypertensives and 300 ± 28 μmol/min (range 221 to 422) in

Table 2. Renal excretory responses to water immersion (WI)

	V/min	$U_{Na}V$	U_KV	π_A
	ml/min	*umol/min*		*mm Hg*
Essential hypertensives				
C	1.3 ± 0.1	111 ± 3	50 ± 8	26.6 ± 0.4
WI (1 hr)	5.6 ± 0.3[a]	331 ± 14[a]	194 ± 18[a]	26.7 ± 0.4
WI (2 hr)	8.7 ± 0.5[a]	535 ± 15[a]	274 ± 26[a]	27.2 ± 0.4
P	0.05	0.05	0.05	NS
Δ(C-2 hr)	+7.4 ± 0.5	+424 ± 14[a]	+224 ± 23[a]	−0.6 ± 0.9
Normotensives				
C	1.1 ± 0.1	99 ± 9	64 ± 8	26.8 ± 0.6
WI (1 hr)	3.4 ± 0.2	157 ± 9	117 ± 13	26.8 ± 0.5
WI (2 hr)	6.9 ± 1.0	300 ± 28	157 ± 22	26.7 ± 0.2
P	0.05	0.05	0.05	NS
Δ(C-2 hr)	+5.8 ± 1.0	+201 ± 25	+93 ± 19	+0.5 ± 0.4

Values are mean ± SEM. $P \leq 0.05$ from C to both first and second hour of WI. Δ(C-2 hr) is positive or negative difference between control condition and 2nd hour of WI.

Abbreviations are: C, control condition; WI, water immersion; V, urine flow; $U_{Na}V$, sodium excretion; U_KV, potassium excretion; π_A, venous colloid osmotic pressure.

[a] Significantly different ($P \leq 0.05$) from corresponding value in normotensive group

Table 3. Effects of central hypervolemia by water immersion (WI) on renal hemodynamic parameters

	C_{In}	ERPF		π_E
	ml/min		FF %	*mm Hg*
Essential hypertensives				
C	108 ± 4	511 ± 11[a]	21 ± 1[a]	38.3 ± 1.2[a]
WI (1 hr)	114 ± 3	694 ± 10	16 ± 0.5	35.4 ± 0.8
WI (2 hr)	111 ± 4	742 ± 12	15 ± 0.4	35.2 ± 0.4
P	NS	0.05	0.05	0.05
Δ(C-2 hr)	+3 ± 1	+231 ± 15[a]	−6.2 ± 0.7[a]	−3.1 ± 1.3
Normotensives				
C	109 ± 4	629 ± 34	17.5 ± 0.5	36.5 ± 0.7
WI (1 hr)	114 ± 4	720 ± 38	15.8 ± 0.7	35.1 ± 0.7
WI (2 hr)	113 ± 4	738 ± 42	15.4 ± 0.5	34.7 ± 0.4
P	NS	0.05	0.05	0.05
Δ(C-2 hr)	+4 ± 1	+109 ± 10	−2.1 ± 0.2	−1.7 ± 0.5

Abbreviatlions are: C_{In}, inulin clearance: C_{PAH}, clearance of p-aminohippurate; FF, C_{In}/C_{PAH}; π_E, efferent arteriolar colloid osmotic pressure; Δ(C-2 hr), positive or negative difference between control condition and 2nd hour of WI.

Values are mean ± SEM. $P \leq 0.05$ from C to both first and second hour of WI.

[a] Significantly different ($P \leq 0.05$) from corresponding value in normotensive group

normotensives ($P < 0.05$). The increase in $U_{Na}V$ from baseline values to second hour of immersion [Δ 0 to 2 hr)] was uniformly much greater in hypertensives, thus showing exaggerated natriuresis in all hypertensives. Both V/min and U_KV were higher during WI in hypertensives with respect to normotensives. Serum protein concentration and derived values of Π_A (Table 2) as well as plasma sodium, potassium and hematrocit (not shown) were not modified by WI.

Renal hemodynamics

Under baseline conditions, ERPF was significantly reduced in our hypertensive patients (511 ± 11 ml/min vs. 629 ± 34 in normotensive controls; $P < 0.05$) (Table 3).

GFR was similar in hypertensive (108 ± 4 ml/min) and normotensive subjects (109 ± 4 ml/min). The FF was significantly increased in hypertensive subjects (21 ± 1%) in comparison with normotensives (17.5 ± 0.5%; $P < 0.05$); Π_E was higher in hypertensives (38.3 ± 1.2 mm Hg) when compared to controls (36.5 ± 0.7 mm Hg; $P < 0.05$).

During WI, GFR was unchanged while ERPF (C_{PAH}) rose significantly in both groups. The ERPF increased during both first and second hour of WI and reached quite identical levels in hypertensive and normotensive subjects; however, the increase from baseline values was greater in the hypertensive than in normotensive group ($P < 0.05$). Consequently, both FF ($P < 0.05$) and Π_E (not significantly) fell during WI to a greater extent in hypertensive than in normotensive subjects.

MAP did not appreciably change in the normotensive group (Table 4), while it significantly fell in hypertensive ($P < 0.05$) versus baseline during both first and second hour of WI. However, MAP remained elevated above normal values, showing a significant difference versus the corresponding MAP in the normotensive group. The time course of MAP in control and hypertensive subjects is represented in Figure 1.

Mean baseline values of IRVP were identical in normotensive (18.2 ± 1.4 mm Hg) and hypertensive subjects (18.0 ± 0.7 mm Hg). IRVP rose during WI reaching a peak value of 32 ± 1.7 mm Hg in normotensives ($P < 0.05$) and of 41 ± 1.4 mm Hg in

Table 4. Effects of water immersion (WI) on mean arterial pressure, intrarenal venous pressure and precapillary resistance

	MAP	IRVP	Precapillary resistance
	mm Hg		*dyne · sec · cm^{-5}*
Essential hypertensives			
C	133 ± 3[a]	18 ± 0.7	10286 ± 433[a]
WI (1 hr)	121 ± 3[a]	34 ± 1.6[a]	5641 ± 241[a]
WI (2 hr)	120 ± 3[a]	41 ± 1.4[a]	4930 ± 130[a]
P	0.05	0.05	0.05
Δ(C-2 hr)	−13 ± 2	−22.8 ± 1.1[a]	−5362 ± 785[a]
Normotensives			
C	91 ± 2	18.2 ± 1.4	5357 ± 363
WI (1 hr)	89 ± 2	29.3 ± 1.5	3816 ± 205
WI (2 hr)	87 ± 2	32 ± 1.7	3378 ± 152
P	NS	0.05	0.05
Δ(C-2 hr)	−7 ± 2	−14 ± 1.2	−1979 ± 784

Abbreviations are: MAP, mean arterial pressure; IRVP, intrarenal venous pressure; Δ(C-2 hr), negative difference between control condition and 2nd hour of WI.

Values as mean ± SEM. $P \leq 0.05$ from C to both first and second hour of WI.

[a] Significantly different ($P \leq 0.05$) from corresponding value in normotensive group

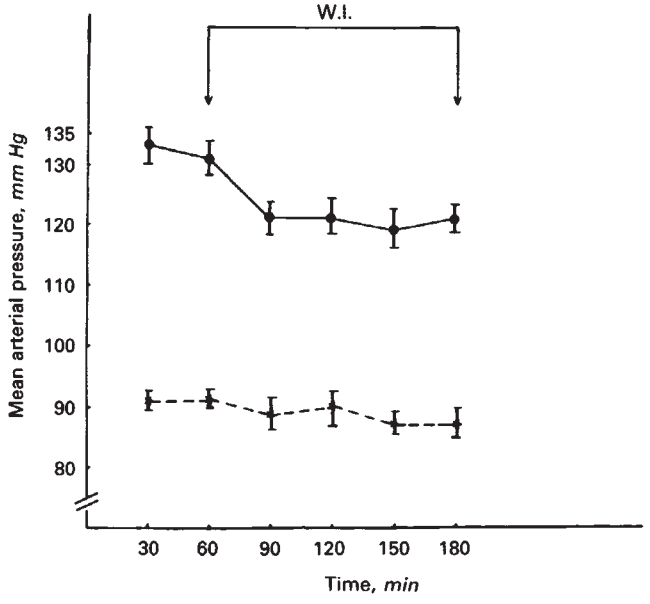

Fig. 1. *Time course of mean arterial pressure before and during water immersion in six normotensive and in six hypertensive subjects.*

hypertensives ($P < 0.05$). IRVP was significantly higher in hypertensives than in normotensives during both first and second hour of WI ($P < 0.05$).

The PVR was significantly elevated during the preimmersion period in hypertensives (10286 ± 433 vs. 5357 ± 363 dyne · sec · cm^{-5}; $P < 0.05$). PVR was markedly reduced during WI in both groups ($P < 0.05$); the fall in PVR was significantly greater during both the first and second hour of WI in hypertensives (−52%) than it was in normotensives (−37%; $P < 0.05$).

Figure 2 represents the mean values of $U_{Na}V$ as a function of IRVP during the basal period, the first and the second hour of WI in six normotensive and six hypertensive subjects.

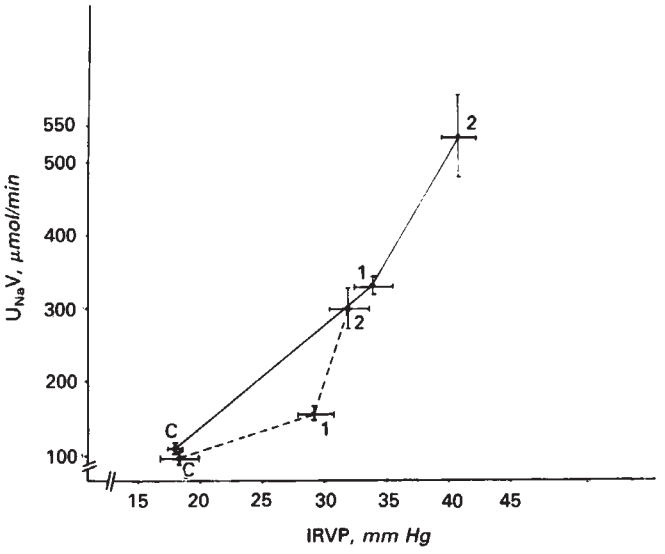

Fig. 2. *Mean values (± SEM) of urinary sodium excretion ($U_{Na}V$) as a function of intrarenal venous pressure (IRVP) (mean values ± SEM) before (C) and at first (1) and second (2) hour of water immersion in six normotensive (dotted line) and six hypertensive subjects.*

Discussion

Under control conditions, diuresis volume and sodium excretion, as well as hematocrit and plasma protein concentration in hypertensives, were not different from those of normotensives. This indicates that both hydration and sodium balance (Table 1) were similar in the two groups.

Our findings show that under basal conditions, IRVP is the same in hypertensive and normotensive subjects. Normal IRVP has been observed by Willassen and Ofstad [15] in hypertensive man, while Lowenstein et al [5] found a substantial increase in IRVP in a group of essential hypertensives. However, these latter authors performed their IRVP measurements during mannitol infusion. Previous observations have shown that IRVP, measured with the present technique (wedged, deep intrarenal venous pressure), may be a satisfactory expression of the hydrostatic pressure in the smallest peritubular capillaries as suggested by Brun et al [16]. In the rat, wedged renal vein pressure closely approximates proximal tubular and peritubular capillary pressure [17]. In the dog, IRVP measurements are comparable to values obtained by direct needle measurements of intrarenal pressure [18]. In both dog [19] and man [5] different maneuvers, known to be able to change periotubular hydrostatic pressure (aortic or renal vein constriction, increase in ureteropelvic pressure, pharmacological renal vasoconstriction or dilation), have been shown to be associated with side changes in IRVP. In the dog, these variations in IRVP have been paralleled by consistent changes in directly needle measured intrarenal pressure [19].

A normal IRVP in hypertensives was associated with a low ERPF and a high PVR, both well-known findings in essential hypertension [20, 21]. This suggests that renal vasoconstriction does not permit the transmission of increased renal perfusion pressure beyond renal arterioles to postglomerular capillaries.

During WI, the renal vasoconstriction was reduced in hyper-

tensive patients who showed a more marked renal vasodilation than control subjects. Furthermore, systemic arterial pressure was significantly reduced by WI in hypertensives, but it remained, by far, more elevated than in the control group. Renal vasodilation was associated with a greater increase in both IRVP and sodium excretion (exaggerated natriuresis) with respect to normotensive subjects. From this, we were able to infer that the transmission of higher systemic pressure to the peritubular capillaries, in the presence of renal vasodilation, produced the more elevated IRVP and subsequently an exaggerated natriuresis in hypertensives during WI. This view well agrees with the suggestion that renal interstitial hydrostatic pressure is the crucial factor linking renal hemodynamic changes to sodium excretion [22, 23].

Both FF and estimated peritubular capillary oncotic pressure (Π_E) were increased in hypertensives under basal conditions [15, 20] and they fell more than in controls subjects with WI, although only FF was statistically significant. However, both FF and Π_E were the same in hypertensives and normotensives throughout WI. Therefore it is very unlikely that transient differences in the time course of FF and Π_E may explain the maximally exaggerated natriuretic response observed during the second hour of WI.

Willassen and Ofstad [15] investigated the possible role of changes in IRVP in hypertensive patients exhibiting exaggerated natriuresis during saline infusion. They concluded that physical factors were not involved in the saline-induced exaggerated natriuresis observed in only a few hypertensive subjects.

However, their experiment, unlike WI, was unable to induce any significant change in IRVP in both control and hypertensive subjects. Thus, it may be difficult to compare results obtained under these two very different experimental conditions. In addition, the MAP of their hypertensives was largely lower (110 ± 3 SEM mm Hg) than that of our hypertensive group. Finally, Lowenstein et al [5] observed that exaggerated natriuresis during saline infusion in hypertensive subjects was associated with a further increase in their baseline elevated IRVP.

Epstein, Loutzenhiser and Levinson [7] recently observed exaggerated natriuresis during WI only in 4 out of their 27 hypertensive subjects. In this subset of hypertensives they found a significant increase in endogenous creatinine clearance during the third hour of WI, while it was unchanged during the first two hours in the presence of marked hypernatriuresis. Consequently, those data clearly confirm that exaggerated natriuresis in hypertensives may occur without significant changes in GFR.

In addition, these authors did not measure blood pressure during WI. Therefore, they were unable to rule out the contribution of changes in the MAP to the variable natriuretic response. Finally, they performed their studies in patients with very restricted sodium intake (10 mEq/day), and a relationship between the reduced basal level of plasma renin activity and the exaggerated natriuretic response to WI emerged from their findings.

Our previous study [8] has shown that exaggerated natriuresis occurs in hypertensives when their MAP values remain elevated during WI. The natriuretic response in those hypertensive patients, showing a fall in MAP toward the normal range during WI, was similar to that measured in normotensive controls. Plasma renin activity and plasma aldosterone were similarly suppressed in hypertensive and control subjects during WI, irrespective of the pressor or natriuretic response [8]. This relationship between high actual MAP and exaggerated natriuresis during volume expansion is in agreement with the previous reports showing that exaggerated natriuresis induced by saline infusion is blunted or abolished during antihypertensive treatment [24, 25].

In conclusion, the present study demonstrates that hypertensive patients exhibit an exaggerated natriuretic response to central volume expansion by WI, at least when their sodium intake is not restricted and their blood pressure remains elevated during WI. Under these experimental conditions, exaggerated natriuresis seems to be well explained by the more marked hemodynamic changes induced by WI in hypertensives. The enhanced renal vasodilation, in the presence of sustained systemic hypertensive, could induce a more pronounced rise in intrarenal venous pressure (that is, peritubular capillary hydrostatic pressure), thus resulting in exaggerated natriuresis.

Reprint requests to Dr. Paolo Coruzzi, Istituto di Semeiotica Medica, Università degli Studi di Parma, Via Gramsci, 14, 43100 Parma, Italy.

References

1. BUCKALEW WM JR, PUSCHETT JB, KINTZEL JE, GOLDBERG M: Mechanism of exaggerated natriuresis in hypertensive man: Impaired sodium transport in the loop of Henle. *J Clin Invest* 48:1007–1016, 1969
2. BALDWIN DS, BIGGS AW, GOLDRING W, HULET WH, CHASIS H: Exaggerated natriuresis in essential hypertension. *Am J Med* 24: 893–902, 1958
3. PAPPER S, BELSKY JL, BLEIFER KH: The response to the administration of an isotonic sodium chloride-lactate solution in patients with essential hypertension. *J Clin Invest* 39:876–884, 1960
4. CANNON PJ: Effects of five per cent dextrose-water infusions in normal and hypertensive man: Evidence for increased proximal and distal tubular sodium rejection by hypertensive patients and its relation to renal hemodynamics. *Circulation* 37:832–846, 1968
5. LOWENSTEIN J, BERANBAUM ER, CHASIS H, BALDWIN DS: Intrarenal pressure and exaggerated natriuresis in essential hypertension. *Clin Sci* 38:359–374, 1970
6. EPSTEIN M: Renal effects of head-out water immersion in man: Implications for an understanding of volume homeostasis. *Physiol Rev* 58:529–581, 1978
7. EPSTEIN M, LOUTZENHISER R, LEVINSON R: Spectrum of deranged sodium homeostasis in essential hypertension. *Hypertension* 8:422–432, 1986
8. CORUZZI P, NOVARINI A, BIGGI A, LAZZERONI E, MUSIARI L, RAVANETTI C, TAGLIAVINI S, BORGHETTI A: Low-pressure receptor activity and exaggerated natriuresis in essential hypertension. *Nephron* 40:309–315, 1985
9. STAHL WM: Renal hemodynamics: The effect of gravity on sodium and water excretion. *Aerospace Med* 36:917–922, 1965
10. CORUZZI P, BIGGI A, MUSIARI L, RAVANETTI C, NOVARINI A: Renal hemodynamics and natriuresis during water immersion in normal humans. *Pflügers Arch* 407:638–643, 1986
11. SCHNURR E, LAHMF W, KUPPERS H: Measurement of renal clearance of inulin and PAH in the steady state without urine collection. *Clin Nephrol* 13:26–29, 1980
12. YOUNG MK, RAISZ LG: An anthrone procedure for determination of inulin in biological fluids. *Proc Soc Exp J Biol Med* 80:771–774, 1952
13. SMITH HW, GOLDRING W, CHASIS H: The measurement of the tubular excretiory mass, effective blood flow and filtration rate in the normal human kidney. *J Clin Invest* 17:263–278, 1938
14. DEEN WM, ROBERTSON CR, BRENNER BM: A model of glomerular ultrafiltration in the rat. *Am J Physiol* 223:1178–1183, 1987

15. Willassen Y, Ofstad J: Renal sodium excretion and the peritubular capillary physical factors in essential hypertension. *Hypertension* 2:771–779, 1980
16. Brun C, Crone C, Davidson HG, Fabricius J, Tybiaerg Hansen A, Lassen NA, Munck O: Renal interstitial pressure in normal and anuric man based on wedged renal vein pressure. *Proc Soc Exp Biol Med* 91:199–202, 1956
17. Gottschalk CW, Mylle M: Micropuncture study of pressure in proximal tubules and peritubular capillaries of the rat kidney and their relation to ureteral and renal venous pressure. *Am J Physiol* 185:430–439, 1956
18. Swann HG, Hink BW, Koester H, Moore V, Prine JM: The intrarenal venous pressure. *Science* 115:64–65, 1952
19. Willassen Y, Ofstad J: Intrarenal venous and cortical catheter pressure in the dog kidney. *Scand J Clin Lab Invest* 39:697–705, 1979
20. London GM, Levenson JA, London AM, Simon AC, Safar ME: Systemic compliance, renal hemodynamics and sodium excretion in hypertension. *Kidney Int* 26:342–350, 1980
21. Hollenberg NK, Borucki LJ, Adams DF: The renal vasculature in early essential hypertension: Evidence for a pathogenetic role. *Medicine (Baltimore)* 57:167–178, 1978
22. Martino JA, Earley LE: Relationship between intrarenal hydrostatic pressure and hemodynamically induced changes in sodium excretion. *Circ Res* 23:371–386, 1968
23. Knox FG, Mertz JI, Burnett JC Jr, Haramati A: Role of hydrostatic and oncotic pressure in renal sodium reabsorption. *Circ Res* 52:491–500, 1983
24. Krauss XH, Schalekamp MADH, Kolsters G, Zaal GA, Birkenhaeger WH: Effects of chronic beta-adrenergic blockade on systemic and hemodynamic responses to hyperosmotic saline in hypertensive patients. *Clin Sci* 43:385–391, 1972
25. Pedersen EB: Effects of sodium loading and exercises on renal hemodynamics and urinary sodium excretion in young patients with essential hypertension before and during propranolol treatment. *Acta Med Scand* 201:365–373, 1977